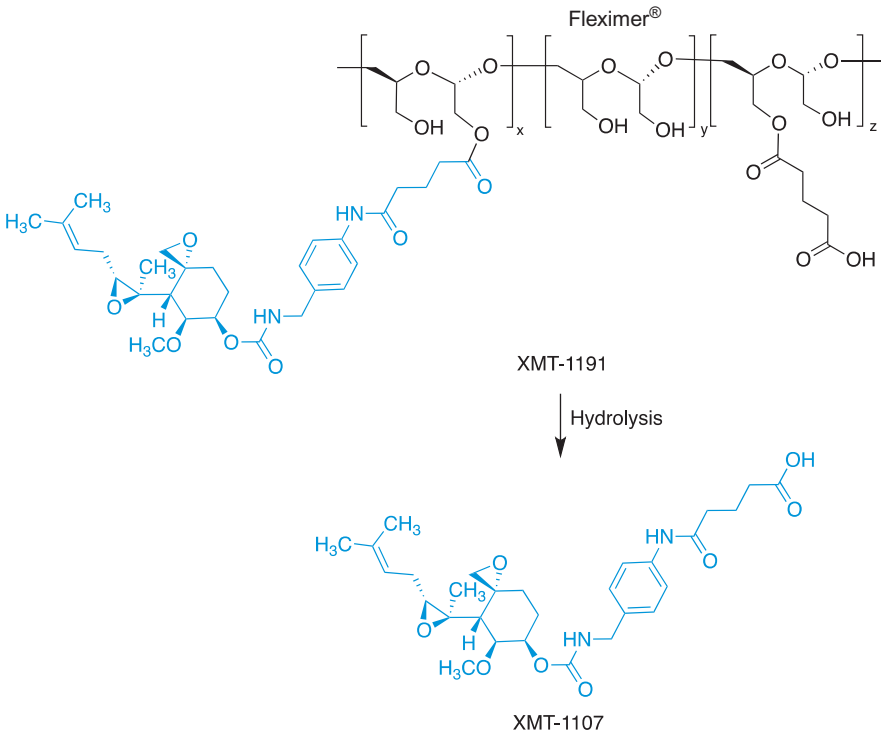

FIGURE 13.34

XMT-1107, a Fleximer®-derived prodrug of XMT-1191.

potential across multiple oncology indications that entered clinical studies in 2010 (Figure 13.34). It has demonstrated dramatically improved pharmacokinetics and no evidence of central nervous system toxicity, establishing it as a potential new antiangiogenic drug with significant therapeutic advantages.[65]

4.5 NEUROPEPTIDE Y CONJUGATES

Receptors of neuropeptide Y (NPY), a 36-amino acid peptide of the pancreatic polypeptide family, are often overexpressed in neuroblastomas. For this reason, conjugates of daunorubicin or doxorubicin with this neuropeptide target and bind to these cells and, after being internalized, release the free drug. Both drugs were covalently linked to NPY via two spacers that differ in stability: an acid-sensitive hydrazone bond at the 13-keto position of daunorubicin and a stable amide bond at the 3′-amino position of daunorubicin and doxorubicin. A Cys residue at position 15 of NPY was used for attaching the maleimide end-moiety of these linkers.[66]